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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,166	12/08/2000	Richard W. Compans	96-99	2363

23713 7590 12/03/2001

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EXAMINER
LI, BAO Q

ART UNIT	PAPER NUMBER
1648	12

DATE MAILED: 12/03/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/733,166	Applicant(s) COMPANS ET AL.	
	Examiner Bao Qun Li	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-20 and 27-28,30-33, 41-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-26, 34-38 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5&6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 21-43 within the scope of a HIV antigen as a target antigen in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the invention has stated the usefulness with bacteria, tumor cells and viruses as target antigens; Applicants respectfully request that all virus, as well as tumor cells and bacterial be examined together. Applicants' argument is fully considered, however, it is not found persuasive. Because each of the claimed virus, bacterial, and tumor cells are structurally and functionally different subject, the searing for different subject constitutes a serious burden both in house and in the commercial data-base for the examiner.

Claims 21-26, 34-38 and 40 directed to the HIV-1 virus as the target antigen are considered by the examiner.

Claims 27-29, 30-33 and 41-43 are not considered because they are directed to the selected HIV-1 as the target virus.

Applicants are reminded to cancel the claims 1-20, 27-29, 33-34, 41-43 and 44-61 to the non-elected group.

Specification

The disclosure is objected to because of the following informalities:

(1). The "inactivated PT8 virus" cited in the Fig. 1 on page 32 should be PR8. Appropriate clarification or correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-26, 34-38 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 is vague and indefinite in that the metes and bonds of " a sialic acids binding component" are not defined. The claim is interpreted in light of the specification, however, specification fails to teach what the definition for the " a sialic acids binding

component" is . Therefore, the claim renders indefinite. This affects the dependent claims.

Claims 21 and 38 are unclear for recitation of " an inactivated or attenuated target cell or virus". While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "an inactivated or attenuated target cell" in claim 21 is used by the claim to mean "target tumor cells that do not cause a tumor or disease in human or animal" while the accepted meaning is a died cells after chemical or physical treatment, e.g. a formalin fixed tumor cells formalin inactivated Mycobacterium Tuberculosis or formalin treated Influenza virus. The attenuated target cells or virus is non-tumorgenic cell lines or replication defective or in-competent mutated virus, such as Adenovirus with E1 to E3 gene deletion or HSV without packaging sequence. This affects the dependent claims 22-26, 34-38 and 40.

Furthermore, the claim renders indefinite in that the metes and bonds of the target cells or virus are not defined. The claim is interpreted in light of the specification; however, since there are many cells and viruses that can be used as the target cells in the art, the claim should point tout which target cell or virus is intended in the said claim. This affects the dependent claims 22-43.

Claim 23 is vague and indefinite in that the metes and bonds of " an inactivated or attenuated preparation of the orthomyxovirus or paramyxovirus" are not defined. The claim is interpreted in light of the specification; however, the specification fails to teach what the definition of "the preparation" is. Is the whole inactivated virus intended or is only certain antigen intended?

Claim 24 is unclear in that the metes and bonds of the sialic acid containing virus preparation are not defined. The sialic acid is a collective term to describe all acylated neuramineic acids. The neuraminic acid is a nine-carbon sugar acid with an amino group in the molecule indicating that it may contains in many kind of the viral preparation. The claims should point out which preparation is intended in the said claim.

Claims 24 and 38 indefinite in that the metes and bonds of " a viral like particle" are not defined. The claim is interpreted in light of the specification, however, the

specification fails to teach which the viral like particle is. Since there are many viral particles in the art, the claim should point out which viral like particle is intended in the said claim.

Claim 25 is indefinite in that the metes and bonds of " an envelope virus" are not defined. Although the claim is interpreted in light of the specification, but the limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181,

Claim 26 is confusing for what the claimed subject is. Is the subject an inactivated tumor cells or a viral preparation. If it is an inactivated tumor cell, the claim is indefinite in that the metes and bonds of " an inactivated tumor cell" are not defined. Although the claim is interpreted in light of the specification, but specification fails to teach what the definition of "an inactivated tumor cell is, and which inactivated tumor cell is intended. Is it is the virus preparation, the claim is unclear for define which antigen preparation of the said virus intended? Is whole HIV virus intended?

In addition, the claims 23, 34 and 37-38 are further confusing for recitation that immuno composition comprising at least one antigen. Since there is no given upper limitation of the antigen in the said claims. Are all antigens from the envelope virus HIV-1 intended? Therefore, the claims are considered as indefinite.

Claim 34 is indefinite in that the metes and bonds of " a sialic acid binding component", " one antigen", a target cell" and "target virus" are all not defined. The claim is interpreted in light of the specification; however, the specification fails to teach specification fails to teach what the definitions for " a sialic acids binding component", " a target cell" and " target virus" are. Since there are many antigens in the art, the claim should point out which antigen is intended in the said claim.

26 USPQ2d 1057 (Fed. Cir. 1993). There are many envelope virus in the art; the claim should point out which envelope virus is intended in the said claim.

Claim Rejections - 35 USC § 112

Claims 21-26, 34-38 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using a formalin-inactivated influenza virus PR/8 for inducing the virus-specific IgM and IgG of all four subclasses in the absence of $CD4^+$ T cell and completely protect the $CD4^+$-deficient mice from the lethal infection

with live, pathogenic influenza virus. does not reasonably provide enablement for having an immunogenic composition comprising any or all sialic acid binding component and any or all inactivated or attenuated tumor cell or viruses or bacterial cells that can produce the same immune response against the any or all specific antigens form the said any or all inactivated or attenuated tumor cell or viruses or bacterial cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants are reminded that the test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors are summarized according to the instant case as following

1) & 2). State of the art and Unpredictable field.

Induction of all classes of IgG antibodies productions in absence of $CD4^+$ T cells with inactivated certain viruses, such as Influenza virus, has been tested in the mice. However, there is no indication that the induced humoral immune response is due to the presence of the sialic acid binding component or sialic acid in the composition tested. The composition comprising HIV-1 antigen inserted in a chimeric influenza virus comprising hemagglutinin (HA) has been tested in animal model only. However, the symptomatic HIV infected patients with Cd4+ T cell deficiency of lymphadenopathy received the inactivated influenza virus remain unprotected from the influenza virus infection, indicating the field is highly unpredictable (Miotti et al. JAMA 1989, Vol. 262, pp. 779-783, See abstract and Table 1-4 on pages 778-782).

Furthermore, in contrary to the claimed invention that any or all inacviated or attenuated virus including the viral like particle that comprises sialic acids or sialci acid binding component are intended to induce Ig class switching in absence of CD4+ T cells,

the state of art art teaches that only T-cell independent antigen (TI) induce the similar effect, but not T-cell dependent antigen (TD) in the absence of the $CD4^+$ T cells. When a viral like particles of repetitive polyomavirus virus are used for immunizing the TCR-βxδ -/- mice or TCR-β -/- mice, the Ig class switching or all classes of Ig production does not observed as evidenced by Szomolanyi-Tsuda et al. (J. Virol. 1998, Vol. 1988, pp. 6665-6670, see entire document), indicating different antigens may behave differently. Therefore, without knowing the characteristic of each individual antigen, it is very unprecidatable whether the composition comprising a sialic acid or a sialic acid binding component in any or all inactivated or attenuated virus, such as HIV, can induce all classes immunoglubulin productions in absence of $CD4^+$ T cells.

In addition, the unpredictability of the claimed invention is also raised for the expected immunity and safety issues because the using formalin or other reagent inactivated vaccine, such as RVS or measles, which are all enveloped virus comprising either sialic acids or sialic acid binding component, cause either enhanced or altered diseases in animals or human being (Murphy et al. vaccine 1990, Vol. 8, pp. 479-502. See entire document, especially the lines 3-11 on the right column of page 470).
3) & 4). Number of working examples and amount of guidance.

The specification only presents that a formalin-inactivated influenza virus PR/8 as an immunogenic composition for inducing the virus-specific IgM and IgG of all four subclasses in the absence of $CD4^+$ T cell and completely protect the $CD4^+$-deficient mice from the lethal infection with live, pathogenic influenza virus. The specification. However, fails to teach that the humoral response is specifically produced by the presence of the sialic acid binding component or the presence of the sialic acid component or other components of the influenza virus. Furthermore, the specification show no working examples in regarding to a composition comprising sialic acid binding component or sialic acid containing viral preparation in combination with an inactivated or attenuated target virus, such as HIV-1, and how the sialic acid binding components is associated with other component of inactivated or attenuated HIV –1 virus. The specification also fail to show that the composition comprising hemogglutinin in combination of other inactivated virus, such as HIV, produce a similar humoral immune response in the $CD4^+$ T-cells deficient situation in vivo . Applicants present no guidance

how the skilled artisan would address and overcome the art recognized problems associated with successful using the said immunogenic composition in the HIV-1 infected AIDS patients, who already had severe impaired function $CD4^+$ T-cells.

5) Scope of the claims,

The invention broadly read on an immunnogenic composition comprising any or all sialic acid biding component and any or all antigen inactivated or attenuated tumor cell or viruses or bacterial cells, such as HIV-1.

6) & 7) Nature of the invention and level of skill in the art.

The invention involves one of the most complex and unpredictable fields of producing an immunogenic composition against any or all kinds of the viruses. Therefore, it requires a high level of the skill in the art to practice the broadly claimed invention.

Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-26 34-38 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Compans (US Patent No. 4,790,987).

Compans disclose vaccine compositions for virus-caused diseases, which including influenza virus, rabies, paramyxovirus, HIV. The composition comprises at least one immunnogenic (F) fusion viral envelope glycoprotein and at least one immunogenic (HN) receptor-biding viral envelope glycoprotein. Although compans does not explicitly indicate that the HN is the sialic acid binding component, the HN include

hemagglutinin and neuraminidase glycoprotein, wherein the hemagglutinin is sialic acid binding component and neuraminidase glycoprotein containing sialic acid because it is glycocylated protein. The vaccine is an attenuated virus comprising part of the whole viral structure and it is inactivated as a virulent strain of the wild type virus (see the entire document). Therefore, the claimed invention is anticipated by the cited prior art.

Claims 21-25, 34-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Pertmer et al. (J. Virol. 1996, Vol. 70, pp. 5119-6125).

Pertmer et al. teach to use a formalin-inactivated influenza virus comprising a hemagglutinin to immunize the mice to produce INF-γ, IL-4 and different classes of the IgG against Influenza neocleoprtein. The hemagglutinin is in the sialic acid binding component and the virus is the formalin-inactivated virus. Therefore, the claimed invention is anticipated by the cited prior art.

Claims 21-26, 34-38 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Muster et al. (J. Virol. 1994, Vol. 68, pp. 4031-4034).

Muster et al. teach a chimeric influenza virus, which comprises an ectodomain of HIV-1 gp41 (ELDKWA) antigen inserted into the loop of antigenic site B of the influenza virus hemogglutinin. The resulting influenza virus comprises a sialic acid binding component hemoglutinin and sialic acid in its envelope glycoprotein. The injection of the said attenuated virus is able to elicit ELDKWA-specific IgG and IgA antisera in mice. Therefore, the claims are anticipated by the cited prior art.

Claims 21-26, 34-38 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Pales et al. (J. Inf. Dis. 1997, Vol. 176 (Suppl 1), pp. S45-S49).

Pales et al. teach several methods for generating attenuated influenza virus vaccines. The first one is made from reassortment of virus through coinfecting cells with virus of circulating strain and attenuated donor influenza virus (e.g. cold-adapted virus, ca). The reassortment viruses are an attenuated influenza virus containing hemogglutinin (HA) and neuraminidase genes (NA). The HA binds to sialic acid and NA comprises sialic acids. The reassortant ca A/Ann Arbor/1/66 viruses administered to thousands of patients induce a long-lasting and highly protective mucosal immune response (see Fig. 1 on page S46 and section: Live virus vaccines: cold-adapted strains). Pales et al. also disclose that the use of an attenuated influenza viral vector to express an HIV-1 gp41

epitope ELDKWA to induce a high level ELDKWA specific IgA on mucosal surface of the respiratory, gastro-intestinal, and genital tracts (see section: Long-lasting mucosal immunity induced by chimeric influenza virus, S47-48)). Therefore, the claimed invention is anticipated by the cited reference.

Claims 21-26, 34-38 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al. (J. Virol. 1993, Vol. 67, pp. 6659-6666).

Li et al. teach a chimeric influenza vector, which expresses a 12-amino acids peptide derived from V3 loop of gp120 of HIV-1. This peptide is inserted into the loop of antigen site B of influenza A/WSN/33 virus hemagglutinin (HA). Mice immunized with the chimeric virus produce anti-HIV antibody and CTL, which recognizes the HIV virus. This vector can be used for inducing both B- and T-cell mediated immunity against other infectious agents. This chimeric influenza virus, is a attenuated influenza virus comprising sialic acid binding component, HA and sialic acid component in the glycoprotein of envelope protein of influenza virus. The attenuated influenza virus also comprises other antigenic component, such as HIV V3 loop antigen. Therefore, the claimed invention is anticipated in the cited reference.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 21-26, 34-38 and 40 are rejected under 35 U.S.C. 102(a) as being anticipated by Chiba et al. (Arch Virol, August 1999, Vol. 144, pp. 1469-1485).

Chiba et al. disclose a recombinant vaccinia virus expressing a chimeric influenza hemagglutinin (HA) protein, wherein the chimeric HA protein comprises 15 residues of the HIV envelope protein gp160. The injection of the said recombinant vaccinia virus (AVV) expressed chimeric HA elicits HIV-specific CTL response and influenza virus specific CTL response as well as anti-influenza HA-specific IgG. The HA is a sialic acid

binding component, the vaccinia virus express many glycoproteins, which inherently comprise sialic acid-containing proteins. The vaccinia virus, HIV-1 virus and influenza viruses used here are all attenuated virus. Therefore, the claimed invention is anticipated by the cited reference.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

November 30, 2001

ALI R. SALIMI
PRIMARY EXAMINER